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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,118	12/30/2003	Richard L. Boyd	NOR-012CP2 and 286336.151	3277

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EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
09/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/749,118	BOYD, RICHARD L.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *34,43,46,51,53-59,61-68,70-78,84-86,91 and 101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-30, 32-33, 36-42, 45, 47-50, 80-82, 92-100 and 103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 29,30,32-34,36-43,45-51,53-59,61-68,70-78,80-82,84-86,91-101 and 103.

DETAILED ACTION

Applicant's amendment filed on 6/16/08 was entered.

Claims 29-30, 32-34, 36-43, 45-51, 53-59, 61-68, 70-78, 80-82, 84-86, 91-101 and 103 are pending in the present application.

This application contains claims 53-59, 61-68, 70-78, 84-86 and 91, drawn to an invention nonelected with traverse in the reply filed on 6/9/2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 34, 43, 46, 51 and 101 (an embodiment) were withdrawn from further consideration because they are directed to non-elected species.

Applicant's elected previously the following species: (a) Leuprolide as a species of disruption of sex-steroid-mediated signaling to the thymus to reactivate the thymus; (b) stem cells as a species of administered cells to the patient; (c) IL-7 as a species of a cytokine; and (d) growth hormone as a species of a growth factor.

Accordingly, amended claims 29-30, 32-33, 36-42, 45, 47-50, 80-82, 92-100 and 103 are examined on the merits herein with the aforementioned elected species.

Response to Amendment

The rejection under 35 U.S.C. 102(e) as being anticipated Slavin, S. (US 6,544,787) and evidenced by Fredrickson et al. (Developmental and Comparative Immunology 18:251-263, 1994; IDS) was withdrawn in light of Applicant's amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Amended claims 29-30, 32-33, 36-42, 45, 47-50, 92-100 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sykes et al. (US 5,658,564; IDS) and in view of Slavin, S. (US 6,544,787), Nowak, R (New Scientist 19/26, page 11, January 2, 1999; IDS) and Mathias, JR (US 5,434,136; IDS) for the same reasons already set forth in the Office action dated 1/17/2008 (pages 5-9). ***The same rejection is restated below.***

Sykes et al disclose at least a method of restoring or inducing immunocompetence or restoring or promoting the thymus-dependent ability for T cell progenitors to mature or develop into functional mature T cells in a host or recipient, including a human adult or a human child, said method comprises the steps of introducing into said host donor thymic tissue, including fetal or neonatal thymic tissue, so that host T cells can mature in the implanted thymic tissue; depleting, inactivating or inhibiting recipient natural killer cells or host T cell function (e.g., introducing antibodies capable of binding to NK cells, T cells and CD4+ cells); irradiating the recipient with low dose, whole body irradiation (e.g., subletthal irradiation, col. 28, lines 47-60); a short course of high dose immunosuppressant such as cyclosporine; as well as recipient

genetically modified hematopoietic stem cells expressing a donor antigen (e.g., a donor MHC gene) to facilitate tolerance to subsequent exposure to donor antigen (see at least Summary of the Invention, particularly col. 1, line 38 continues to line 35 of col. 3 and issued claims). Please be noted that a recipient receiving donor thymic tissue, particularly fetal or neonatal thymic tissue, falls within the scope of a patient with a thymus undergoing reactivation. **Sykes et al also teach the same method is used for treating a human at risk for an acquired immune disorder such as AIDS, patients suffering from an immunodeficiency such as a T cell deficiency, immunoincompetence resulting from a neoplastic disease or immunoincompetence resulting from a medical procedure such as chemotherapy or radiation treatment** (col. 15, lines 31-39).

Sykes et al further teach that due to the discovery that hematopoietic stem cells can be used to induce tolerance to a graft, they disclose a method for inducing immunological tolerance in a recipient mammal, including a human adult or a human child, of a first species to a graft obtained from a donor mammal of a second species, said method comprises prior to or simultaneous with transplantation of the graft, introducing into the recipient mammal hematopoietic stem cells of the second species; depleting, inactivating or inhibiting recipient natural killer cells or host T cell function (e.g., introducing antibodies capable of binding to NK cells, T cells and CD4+ cells); irradiating the recipient with low dose, whole body irradiation (e.g., subletthal irradiation, col. 28, lines 47-60); and a short course of high dose immunosuppressant such as cyclosporine (col. 11, line 16 continues to line 16 of col. 13; and particularly issued

claims 21-24). Sykes et al disclose that although hematopoietic stem cells derived from the graft donor are preferable, hematopoietic stem cells may be obtained from other individuals or species, or from genetically-engineered completely or partially inbred donor strains (col. 27, lines 34-37).

Sykes et al do not teach explicitly that the above methods to be used for treating a patient having or suffering an autoimmune disease; and specifically the use of Leuprolide, an LHRH agonist, **(the elected species)** for restoring or inducing immunocompetence or restoring or promoting the thymus-dependent ability for T cell progenitors to mature or develop into functional mature T cells in a host or recipient, even though Sykes et al disclose specifically that their methods can be use to treat a human at risk for an acquired immune disorder such as AIDS, patients suffering from an immunodeficiency such as a T cell deficiency, immunoincompetence resulting from a neoplastic disease or immunoincompetence resulting from a medical procedure such as chemotherapy or radiation treatment.

However, at the effective filing date of the present application Slavin already taught a method for treating a human patient with a pathogenic cell disease, including an autoimmune disease, said method comprises an intense lymphoablative regimen, an submyoalative regimen and transplantation of a donor-derived preparation that includes allogeneic stem cells that are obtained at least from bone marrow, mobilized peripheral blood or cord blood (see at least Summary of the Invention, and section entitled "Method 1" in cols. 5-10).

Additionally, Nowak already reported that temporary chemical castration could help regenerate the damaged immune systems of people with HIV or who have had chemotherapy or bone marrow transplants. Nowak further disclosed that the work of Drs. Boyd and Sutherland demonstrated that upon castration, thymus of adult mice regained its youthful appearance within four weeks and the number of T cells produced increased to near pre-pubertal levels, suggesting that drugs (e.g., LHRH or luteinising hormone-releasing hormone) that suppress the production of sex steroids and partially reverse puberty might boost the immune systems of patients with AIDS or those who gave been given immunosuppressive drugs.

Furthermore, Mathias already taught the use of GnRH analogs, particularly Lupron or luprolide acetate due to its increased biologic activity, stability against enzymatic degradation and high binding affinity for GnRH receptors, **for alleviating the debilitating symptoms of motility disorders such as systemic lupus erythematosis, autonomic neuropathies of diabetes mellitus, sclerroderma, Parkinson's disease, functional bowel disease at least via their inhibitory activity against the production of reproductive hormones** (see at least Summary of the Invention, particularly col. 3, lines 34-46 and 53-60; col. 2, lines 52-62). Mathias further disclosed that GnRH and its analogs are routinely used in the treatment of disorders of the reproductive system, including patients with endometriosis, hormone-dependent tumors such as prostatic mammary carcinomas, polycystic ovarian disease (col. 4, lines 48-62).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time of invention was made to modify the teachings of Sykes et al. by also treating a patient having or suffering an autoimmune disease as well as administering leuprolide to the treated patient in light of the totality of the teachings of Slavin, Nowak, and Mathias as presented above.

An ordinary skilled artisan would have been motivated to carry out the above modification to restore or promote the thymus-dependent ability for T cell progenitors to mature or develop into functional mature T cells in a host or recipient having or suffering from an autoimmune disease, who is also normally subjected to an intense lymphoablative regimen (a chemotherapy), an submyoalative regimen that includes low-dose ionizing irradiation delivered by an exogenous radiation source as well as allogeneic stem cell transplantation for treatment as taught by Slavin. Please note that Sykes et al disclose specifically that their methods can be use to treat any human suffering immunoincompetence resulting from a medical procedure such as chemotherapy or radiation treatment. Furthermore, Nowak discloses that drugs (e.g., LHRH or luteinising hormone-releasing hormone) that suppress the production of sex steroids and partially reverse puberty might boost the immune systems of patients with AIDS or those who gave been given immunosuppressive drugs, and that GnRH and its analogs such as leurpolide have been used safely in humans for various treatments, including patients with disorders of the reproductive system as well for alleviating the debilitating symptoms of motility disorders such as systemic lupus erythematosis, autonomic neuropathies of diabetes mellitus, sclerroderma, Parkinson's disease,

functional bowel disease at least via their inhibitory activity against the production of reproductive hormones as taught by Mathias. The resulting modified method is indistinguishable from the method as claimed because it has the same method steps and starting materials.

An ordinary skilled artisan would have a reasonable expectation of success because in light of the teachings of Sykes et al., Slavin, Nowak, and Mathias; coupled with a high level of skill of an ordinary artisan in the relevant art.

Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments with respect to the above rejection in the Amendment filed on 6/16/08 (pages 14-18) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

1. Applicant argues that the combination of cited references fails to disclose all the elements of Applicant's claims because the combined references fail to teach the treatment of a patient with autoimmune disease by reactivating the thymus of the patient wherein the thymus is reactivating by disruption of sex-steroid signaling to the thymus.

Please note that the above rejection is made under 35 U.S.C. 103(a); and therefore none of the cited references has to teach every element of the claims. The combined references teach every element of the instant broad claims which are further discussed below.

2. Applicant argues the primary Sykes reference does not refer to two essential features of the claimed invention, namely treating an autoimmune disease and reactivating the thymus of the patient, particularly Sykes teaches providing thymic tissue from a source other than the patient. Applicant also argues that unlike Sykes' method, Applicant's invention relates to reactivating the existing thymus of the patient. With respect to the Slavin secondary reference, Applicant argues that this reference relates to methods for reducing anti-donor responsiveness in treating various diseases, including autoimmune diseases, but it does not mention the benefits of reactivating the patient's thymus to treat an autoimmune disease. With respect to the Novak reference, Applicant argues that it is a second hand information written by a journalist which provides no scientific data and it does not mention treating autoimmune disease, let alone the additional step of depleting T cells in the patient or providing the patient with immunosuppressive therapy prior to reactivating the thymus. Finally, with respect to the Mathias reference, Applicant argues that this reference relates to treating motility disorders and that motility disorders are "secondary disorders associated with autoimmune disorders"; and that this reference does not teach or suggest treating an autoimmune disease per se, let alone depleting T cells in a patient and reactivating the thymus of a patient with an autoimmune disease by disruption of sex steroid mediated signaling to the thymus. In sum, the cited references do not teach or suggest reactivating the existing thymus of the patient to treat an autoimmune disease.

Firstly, it appears that Applicant considers the teachings of each of the cited references in total isolation one from the others.

Secondly, it should be noted that as written the instant broad claims **are not necessarily limited only to reactivating endogenous or existing endogenous thymus of a patient having or suffering an autoimmune disease as argued by Applicant.** Furthermore, it should be noted that **the claimed methods also contain the open language of the term "comprising" meaning that that the methods can contain additional steps**. After the implantation, the donor thymus belongs to the treated patient in the method taught by the Sykes reference and it is a body part of the treated patient, and therefore it is within the broad scope of "the thymus of the patient". Moreover, please also note that **an embodiment of the Sykes' teachings include a method for inducing immunological tolerance in a recipient mammal, including a human adult or a human child, of a first species to a graft; not necessarily limited to a thymus, obtained from a donor mammal of a second species**, said method comprises prior to or simultaneous with transplantation of the graft, introducing into the recipient mammal hematopoietic stem cells of the second species; depleting, inactivating or inhibiting recipient natural killer cells or host T cell function (e.g., introducing antibodies capable of binding to NK cells, T cells and CD4+ cells); irradiating the recipient with low dose, whole body irradiation (e.g., subletthal irradiation, col. 28, lines 47-60) **due to the discovery that hematopoietic stem cells can be used to induce tolerance to a graft**. Therefore, **the recipient mammal in such a method does not have its endogenous thymus to be depleted or removed**.

Thirdly, the Slavin reference teaches clearly **a method for treating a human patient with an autoimmune disease comprising the step of transplanting a donor-derived preparation that includes allogeneic stem cells that are obtained from bone marrow, mobilized peripheral blood or cord blood**. Therefore, this teaching is relevant to the teachings of the primary Sykes reference, and it is one of the threads to combine the cited references **to render the instant broadly claimed invention as a whole was *prima facie* obvious.**

Fourthly, **Nowak reference is clearly a prior art reference**. It reported explicitly the important finding that **temporary chemical castration could help regenerate the damaged immune systems of people with HIV or who have had chemotherapy or bone marrow transplants**. Nowak further disclosed that **the scientific work of Drs. Boyd and Sutherland** demonstrated that upon castration, thymus of adult mice regained its youthful appearance within four weeks and the number of T cells produced increased to near pre-pubertal levels, **suggesting that drugs (e.g., LHRH or luteinising hormone-releasing hormone) that suppress the production of sex steroids and partially reverse puberty might boost the immune systems of patients with AIDS or those who gave been given immunosuppressive drugs.**

Fifthly, with respect to the Mathias reference it is noted that **treating motility disorders which are secondary disorders associated with autoimmune disorders** falls within a broad scope of "treating or alleviating symptoms of an autoimmune disease" in a patient of the methods as claimed. Nevertheless, Mathias stated "The present invention relates to the treatment of functional motility disorders including

diseases of the autonomic nervous system of idiopathic or known causes. **Treatment of Functional Bowel Disease or disease of the irritable bowel, as well as the autonomic dysfunction of autoimmune diseases such as Systemic Lupus Erythematosus (SLE) with an analog of GnRH is disclosed**". Any reasonable person would clearly understand that Mathias teaches a treatment method at least for SLE, an autoimmune disease, using an analog of GnRH.

In Sum, the combined teachings of Sykes et al., Slavin, Nowak, and Mathias meet every limitation of the instant broad claims, and motivations have been provided in the above rejection to render the claimed invention as a whole was *prima facie* obvious.

3. Applicant also argues that the Office action's proposed modification (reactivating the thymus of the patient) would modify Sykes's principle of operation which based on permitting host T cells to mature in donor thymic tissue. Such a modification would not be *prima facie* obvious.

The modified method resulting from the combined teachings of Sykes et al, Slavin, Nowak and Mathias as set forth above do not modify Sykes's principle of operation in any shape or form. Please refer to the Examiner's interpretation of the instant broad claims as well as the totality of the teachings of Sykes as discussed immediately preceding paragraphs.

4. Applicant further argues that the rejection was based on hindsight analysis, without providing any scientific reason why the skilled person would have been

motivated to modify in a significant manner the teachings of Sykes. Finally, even if the references were to be combined as set forth in the Office action, there is simply no expectation of success since there is simply no teaching in the combined references that reactivating the thymus of the patient would lead to treating a patient with an autoimmune disease.

Firstly, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. **But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper**. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Secondly, an ordinary skilled artisan would have a reasonable expectation of success because in light of the teachings of Sykes et al., Slavin, Nowak, and Mathias; coupled with a high level of skill of an ordinary artisan in the relevant art. At least Slavin already disclosed a successful method for treating a human patient with an autoimmune disease; Mathias also taught successfully a treatment method at least for SLE, an autoimmune disease, using an analog of GnRH as well as in light of the finding s and suggestions resulting from **the scientific work of Drs. Boyd and Sutherland** reported by Nowak.

Accordingly, amended claims 29-30, 32-33, 36-42, 45, 47-50, 92-100 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sykes et al. (US 5,658,564; IDS) and in view of Slavin, S. (US 6,544,787), Nowak, R (New Scientist

19/26, page 11, January 2, 1999; IDS) and Mathias, JR (US 5,434,136; IDS) for the same reasons already set forth in the Office action dated 1/17/2008 (pages 5-9).

Amended claims 80-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sykes et al. (US 5,658,564; IDS) and in view of Slavin, S. (US 6,544,787), Nowak, R (New Scientist 19/26, page 11, January 2, 1999; IDS) and Mathias, JR (US 5,434,136; IDS) as applied to claims 29-30, 32-33, 36-42, 45, 47-50, 92-100 and 103 above, and further in view of Bolotin et al. (Blood 88:1887-1894, 1996; IDS) for the same reasons already set forth in the Office action dated 1/17/2008 (pages 10-11). ***The same rejection is restated below.***

The combined teachings of Sykes et al, Slavin, Norwak and Mathias were disclosed above. However, none of the references specifically teaches a further step of administering IL-7 (the elected species) in any of the disclosed methods.

However, at the effective filing date of the present application Bolotin et al already taught that IL-7 administration promotes thymic reconstitution and enhanced thymopoiesis after bone marrow transplantation (BMT) and is useful in preventing post-bone marrow transplantation immune deficiency (see at least the abstract).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time of invention was made to further modify the combined teachings of Sykes et al, Slavin, Norwak and Mathias by further administering IL-7 into the treated host in light of the teachings of Bolotin et al.

An ordinary skilled artisan would have been motivated to carry out the above modification to enhance thymopoiesis and thereby restoring or promoting the thymus-dependent ability for T cell progenitors to mature or develop into functional mature T cells, as well as preventing post bone marrow transplantation immune deficiency in the treated patients.

An ordinary skilled artisan would have a reasonable expectation of success because in light of the teachings of Sykes et al, Slavin, Norwak, Mathias and Bolotin et al., coupled with a high level of skill of an ordinary artisan in the relevant art.

Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments with respect to the above rejection in the Amendment filed on 6/16/08 (page 19) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

Applicant argues that the instant claims are not directed to improving engraftment after bone marrow transplantation, but rather to a method for treating or alleviating symptoms of an autoimmune disease in a patient having or suffering an autoimmune disease. Accordingly, the Bolotin reference does not cure the deficiencies of the combined teachings of Sykes, Slavin, Nowak and Mathias references for the reasons set forth above.

With respect to the deficiencies of the combined teachings of Sykes, Slavin, Nowak and Mathias references, please refer to the Examiner's rebuttals to Applicant's arguments for the rejection of claims 29-30, 32-33, 36-42, 45, 47-50, 92-100 and 103 above. It should be noted that the Bolotin reference is cited to supplement the combined teachings of Sykes, Slavin, Nowak and Mathias for a method containing a further step of administering IL-7.

Amended claims 80 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sykes et al. (US 5,658,564; IDS) and in view of Slavin, S. (US 6,544,787), Nowak, R (New Scientist 19/26, page 11, January 2, 1999; IDS) and Mathias, JR (US 5,434,136; IDS) as applied to claims 29-30, 32-33, 36-42, 45, 47-50, 92-100 and 103 above, and further in view of Tian et al. (Stem Cells 16:193-199, 1998; Cited previously) for the same reasons already set forth in the Office action dated 1/17/2008 (pages 11-12). ***The same rejection is restated below.***

With respect to the elected species, the combined teachings of Sykes et al., Slavin, Nowak and Mathias were presented above. However, none of the references specifically teaches a further step of administering a growth hormone (elected species) in any of the disclosed methods.

However, at the effective filing date of the present application Tian et al already taught at least that a recombinant human growth hormone administration promotes hematopoietic reconstitution after syngeneic bone marrow transplantation (BMT) and is

of clinical useful for accelerating hematopoiesis after autologous BMT (see at least the abstract).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time of invention was made to further modify the combined teachings of Sykes et al., Slavin, Nowak and Mathias by further administering a recombinant human growth hormone into a treated patient in light of the teachings of Tian et al.

An ordinary skilled artisan would have been motivated to carry out the above modification to enhance hematopoiesis, including platelet recovery, through enhanced hematopoietic reconstitution in the treated patients as taught by Tian et al.

An ordinary skilled artisan would have a reasonable expectation of success because in light of the teachings of Sykes et al., Slavin, Nowak and Mathias and Tian et al., coupled with a high level of skill of an ordinary artisan in the relevant art.

Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments with respect to the above rejection in the Amendment filed on 6/16/08 (page 20) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

Once again, Applicant argues that the instant claims are not directed to improving engraftment after bone marrow transplantation, but rather to a method for

treating or alleviating symptoms of an autoimmune disease in a patient having or suffering an autoimmune disease. Accordingly, the Tian reference does not cure the deficiencies of the combined teachings of Sykes, Slavin, Nowak and Mathias references for the reasons set forth above.

With respect to the deficiencies of the combined teachings of Sykes, Slavin, Nowak and Mathias references, please refer to the Examiner's rebuttals to Applicant's arguments for the rejection of claims 29-30, 32-33, 36-42, 45, 47-50, 92-100 and 103 above. It should be noted that the Tian reference is cited to supplement the combined teachings of Sykes, Slavin, Nowak and Mathias for a method containing a further step of administering a growth hormone.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Amended claims 29-30, 32-33, 36-37, 39-42, 45, 47-50, 80-82, 92, 94-100 and 103 are provisionally rejected under the judicially created doctrine of obviousness-type

double patenting as being unpatentable over claims 19-20, 23, 25, 28-31, 34-36, 38-40, 55, 57-60, 62, 64, 66 and 68 of copending Application No. 10/749,119 for the same reasons already set forth in the Office action dated 1/17/2008 (pages 13-14). ***The same rejection is restated below.***

Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are directed to a method for treating or alleviating symptoms of an autoimmune disease in a patient having or suffering an autoimmune disease, comprising the steps of depleting T cells in the patient; and reactivating the thymus of the patient. Claims 19-20, 23, 25, 28-31, 34-36, 38-40, 55, 57-60, 62, 64, 66 and 68 of copending Application No. 10/749,119 are drawn to a method for inducing tolerance in a patient to a graft from a mismatched donor, comprising the steps of depleting T cells of the patient or providing the patient with immunosuppressive therapy, reactivating the thymus of the patient and administering cells from the mismatched donor to the patient, wherein the cells being selected from the group consisting of stem cells, progenitor cells, dendritic cells, and combinations thereof.

The claims of the present application differ from the claims of the co-pending application in reciting "treating or alleviating symptoms of an autoimmune disease in a patient having or suffering an autoimmune disease". The claims of the present application can't be considered to be patentably distinct over claims 19-20, 23, 25, 28-31, 34-36, 38-40, 55, 57-60, 62, 64, 66 and 68 of copending Application No. 10/749,119 when the co-pending application teaches specifically that the treated patient includes one having any T cell disorder, including Lupus-like symptoms or type I diabetes having

thymic abnormality (see at least page 10, lines 1-2; and page 2, line 25 continues to line 6 of page 3), and therefore they fall within the scope of claims 29-33, 36-37, 39-42, 45, 47-50, 80-82, 92, 94-100 and 103 of the present application. This is because it would have been obvious to an ordinary skilled artisan to modify the method of the co-pending application for treating autoimmune disease in a patient having or suffering an autoimmune disease to support the instant claims.

An ordinary skilled artisan would have been motivated to do this because this embodiment is apparently disclosed as one of the preferred embodiments.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicants' arguments with respect to the above rejection in the Amendment filed on 6/16/08 (page 21) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

Applicants argue simply that the claims of the co-pending Application 10/749,119 are directed to methods for inducing tolerance in a patient to a graft from a mismatched donor, and that these claims do not teach or suggest or motivate one ordinary skilled artisan to arrive at the presently amended claims even thought the steps recited in the two applications may be similar or that the patient pool may include similar patients.

Once again, the claims of the co-pending Application 10/749,119 have the same method steps as those of presently amended claims. Furthermore, the claims of the

present application can't be considered to be patentably distinct over claims 19-20, 23, 25, 28-31, 34-36, 38-40, 55, 57-60, 62, 64, 66 and 68 of copending Application No. 10/749,119 when **the co-pending application teaches specifically that the treated patient includes one having any T cell disorder, including Lupus-like symptoms or type I diabetes having thymic abnormality** (see at least page 10, lines 1-2; and page 2, line 25 continues to line 6 of page 3), and therefore they fall within the scope of claims 29-33, 36-37, 39-42, 45, 47-50, 80-82, 92, 94-100 and 103 of the present application. Therefore, it would have been obvious to an ordinary skilled artisan to modify the method of the co-pending application for treating autoimmune disease in a patient having or suffering an autoimmune disease to support the instant claims. An ordinary skilled artisan would have been motivated to do this because this embodiment is apparently disclosed as one of the preferred embodiments.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN, Ph.D./
Primary Examiner, Art Unit 1633